REMARKS/ARGUMENTS

Receipt of the Office Action mailed December 10, 2003 is acknowledged. Claims 1-4 and 12-20 remain in this application. Claims 5-17 have been canceled without prejudice or disclaimer. Claim 1 has been amended. Support for the amendment to claim 1 can be found throughout the original disclosure. No new matter has been entered. Entry of the amendment is respectfully requested.

1. Drawings

Applicants note with appreciation that the Examiner has approved the drawing correction enclosed with the previous reply.

2. Section 112, First Paragraph Rejection

In paragraph 2 of the Office Action, claims 1-4 stand rejected under 35 U.S.C. 112, first paragraph as "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Reconsideration and withdrawal of the rejection are respectfully requested.

The Examiner argues there is no support in the original disclosure for detecting failures that can result from *multiple failure modes*. The Examiner takes the position that the original disclosure provides support for multiple detection schemes for the same failure, referring to the instant specification at page 7, lines 22-29 for support, noting "by taking advantage of the multiplying effect of multiple detection schemes targeting the

same failure mode, each detection scheme does not have to be extremely robust in order to achieve a robust detection system."

Before addressing the rejection, applicants believe that a brief review of the invention including a description of failure modes and detection schemes would be helpful in understanding how the applicants had possession of what is being claimed. The present invention is premised on the discovery that biased or incorrect results (i.e., assay failures) in an analyzer can be significantly reduced by first identifying potential sources of the failure (i.e., failure modes). An example of a failure (or error) is failure of the reagent management system as described in the specification at page 18, line 26. An example of a failure mode (or potential sources of errors) is the plugged reagent probe, described at page 18, line 31. Identifying failure modes is succinctly described in the specification at page 15, line 28 to page 16, line 3:

> Once an analyzer is conceptually categorized according to systems and subsystems, ***potential sources of error are identified within each***. That is, problems that do or can arise are linked to actual or possible error sources within the systems. For example, a failure could occur if an ineffectual quantity of reagent is used in the assay. Possible causes of such an event include, for example, an occluded reagent probe, clogged fluidic components, failure to detect empty or near empty reagent packs, false level sensing of fluid due to bubble formation on the top of the fluid, incorrect alignment of dispense systems during aspiration or dispensing. (Emphasis added).

Once the failure (e.g., reagent metering failure) and the failure mode are identified, then it becomes necessary to determine if the failure mode (e.g., occluded reagent probe) will have a significant effect on the result. That is, not every failure mode is likely to result in a clinically significant error based on the effect the error has and the probability that such an error will occur, and thus, not worth the effort to detect the failure mode. Again this step is described in the specification at page 16, lines 4 to 12:

> The effect of each such cause is then quantified so that the extent of the contribution to a failure is associated with each possible cause. For example, a

> completely occluded reagent probe would result in a complete failure while a leaky pump would only affect the accurate dispensing of reagent by 0-50 %. Likewise, the probability of each possible cause is quantified. This is done by evaluating usage data or by reiterative testing of the function of the component identified as a possible cause. For example, one can determine the statistically relevant number of occurrences of reagent aspiration that would be needed to determine the frequency of reagent probe occlusion and then actually conduct that number of operations to arrive at a measure of the probability of such an event.

Finally, multiple error detection measures are identified, selected and implemented to reduce errors to an acceptable limit along with a low probability of false detection of an assay failure. This is illustrated in the specification at page 17, lines 7-20:

> In detecting failures in the reagent metering operation a volumetric verification that checks fluidics can be performed on start-up that has an error probability of about 1 in 100. By adding another failure detection scheme during a wash step that verifies that the reagent probe has not been clogged another reduction of 1 in 100 probability of failing to detect a reagent metering problem is attained. Further, another 1 in 100 probability of failing to detect such a failure is attained by measuring the volume of a well once reagents and sample have been dispensed in it. This multi-level approach makes it possible to have detection processes that have an overall false negative frequency of less than 1 in 1,000,000 (i.e., 100^3). If however, one or more of the proposed detection schemes would introduce a higher rate of false positives (i.e., it would be too sensitive) relative to other possible detection schemes, then one would employ the combination of schemes that would give the acceptable false negative rate with the lower false positive rate. This process permits a high rate of confidence in detecting failures without having to employ every possible means of failure detection.

This section of the specification describes a failure (e.g., failures in reagent metering operation) and failure modes (e.g., clogged reagent metering probe). Also described are multiple detection schemes (i.e., 1) checking fluidics on start up, 2) clog detection during the wash step, and 3) measuring the volume of a well). Assuming that each of these detection schemes has a 1 in 100 probability of failing to detect a reagent

metering probability, the failure that all three will fail to detect a problem is 1 in 1,000,000. Thus, by selecting multiple detection schemes the rate of failing to detect falls to an acceptable level. Also, if the detection scheme would result in an unacceptable rate of false positives, then other combinations of detection schemes could be used besides the scheme providing too many false positives.

Turning now to the Examiner's rejection, applicants point out that the present specification provides ample support for detecting failures that can result from multiple failure modes. As described above, multiple failure modes can include, for example, an occluded reagent probe, clogged fluidic components, failure to detect empty or near empty reagent packs, false level sensing of fluid due to bubble formation on the top of the fluid, incorrect alignment of dispense systems during aspiration or dispensing.

Moreover, the paragraph bridging the specification at pages 18 and 19 describe seven possible failure modes that can occur in the embodiment for failure to the reagent management system. Likewise, the table at page 28 shows failures (i.e., no delivery of reagent and no delivery of diluent) and failure causes. Accordingly, the disclosure, as filed, provides adequate written description for the claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

Section 112, Second Paragraph Rejection

In paragraph 5 of the Office Action, claims 1-4 stand rejected under 35 U.S.C. 112, second paragraph as being indefinite for recital of the term "can" in the claims. In view of the amendment to the claims, applicants submit that the rejection has been obviated. Accordingly, applicants submit that claims 1 to 4 satisfy section 112, second paragraph.

Section 102(b) rejections

In paragraphs 9 and 10 of the Office Action, claims 1-4 stand rejected under 35 U.S.C. 102(b) as being anticipated Farmer, U.S. Patent No. 5,315,529 ("Farmer"). In view of the foregoing amendments and the remarks that follow, reconsideration and withdrawal of the rejections are respectfully requested.

With regard to Farmer, the claims have been amended to recite the multiple failure modes within the body of the claim. The use of "can" in the claims has been deleted, thus, the recitation in the claims of "multiple failure modes" must be given patentable weight. As noted in previous replies, Farmer is directed entirely to external monitoring of fluid vessels such as by the placement of sensors in the environment around the vessel. *See* col. 1, line 42; col. 3, line 1. The methods, systems and devices described in the patent are all directed to detecting one type of event in a fluid containment vessel, namely, a leak. Errors that can result from assay failure that are not leaks (e.g., dilution errors) cannot be determined because there are no events that are detected other than leaks. Indeed, Farmer is not directed to assay failure at all, let alone assays for which failures can be detected.

In addition, the steps of "selecting and implementing multiple error detection measures for each failure mode based on their probability of reducing errors to an acceptable limit along with a low probability of the false detection of an assay failure" does not occur in and is not suggested by Farmer. Instead, Farmer teaches that "[i]n general, the greater number of sensors 30 utilized increase the speed with which leaks 60 may be detected and also increase confidence that a leak 60 will not be missed by the sensors." *See* col. 5, line 22. This is a "more is better" approach commonly seen in the prior art. It is inapposite with the approach taken in the present application. Here, failure detection measures take advantage of the statistical relevance of the pathway in which the failure modes occur. This allows one to increase the probability of detecting a failure without necessarily relying on an abundance of sensors, the proliferation of

which results in increased false reports of errors. *See* page 5, line 12 of the present application. Since among other things, Farmers does not contain the claim elements described above, Farmer cannot anticipate the claimed invention.

Since Farmer fails to teach or suggest multiple failure modes or their detection, reconsideration and withdrawal of the rejection are respectfully requested.

Based on the foregoing, applicants believe the application is now in condition for allowance. Favorable reconsideration and notice of allowance are solicited. If any questions arise which can be disposed through interview, the Examiner is encouraged to contact Applicants' attorney at the telephone number listed below.

Please charge any fees which may be required for this submission to Johnson & Johnson Deposit Account No. 10-0750/CDS-215/TJB.

Respectfully submitted,

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